REMARKS/ARGUMENTS

Status of the claims

Claims 1 to 31 were previously pending and presented for examination. Claims 1 to 10, 12, 13, 18, 19, 23, 30, and 31 are herein amended. Claims 11, 14 to 17, 20 to 22, and 24-29 are canceled without prejudice. Claims 32 to 39 are newly submitted. After entry of these amendments, claims 1 to 10, 12, 13, 18, 19, 23, and 30 to 39 will be pending.

Support for the amendments to the claims

Claim 1 was amended in order to clarify the composition of the chemical compounds that comprise the combination reaction products. Support for the amended language can be found, for example, in lines 5 to 13 on page 7 of the specification.

Claims 2 and 9 were amended to set forth preferred embodiments in which the self-assembly moieties of the chemical compounds comprise oligonucleotides or functional analogues thereof. Support for these amendments can be found in the original presentation of claims 2 and 9.

Claims 3 and 10 were amended in order to better define the composition and use of the linking chemical compounds. Support for these amendments can be found, for example, in the paragraph bridging pages 15 and 16 of the specification.

Claims 4 to 7, 12, and 13 were amended in order to properly not refer to a figure in a claim.

Claims 8 and 18 were amended to clarify that the claimed library comprises members of the chemical compounds described in claim 1.

Claim 19 was amended in order to properly not multiply depend upon claims 1 to 7. Additionally, this claim was amended to set forth preferred embodiments of the self-assembly moiety. Support for these embodiments can be found, for example, in lines 21 to 25 on page 13 of the specification for oligonucleotides, in lines 27 and 28 on page 13 of the specification for polypeptides, and in lines 30 to 34 on page 13 of the specification for metal-binding ligands.

Claim 23 was amended in order to set forth preferred embodiments of the chemical moieties such that they are attached to the oligonucleotides as iodoacetamido- or maleido-derivatives. Support for these embodiments can be found, for example, in lines 31 to 34 on page 9 of the specification.

Claim 30 has been amended as to update its dependency and to set forth preferred embodiments of the method in which the chemical compounds comprise heterotrimers and heterotetramers. Support for these embodiments can be found, for example, in lines 19 to 24 on page 9 of the specification.

Claim 31 has been amended as to update its dependency.

Claims 32 and 33 are newly presented to set forth preferred embodiments of the self-assembly moiety. Support for these claims can be found, for example, in lines 30 to 34 on page 13 of the specification with respect to claim 32, and in lines 27 and 28 on page 13 of the specification with respect to claim 33.

Claims 34 to 36 are newly presented to set forth preferred embodiments of the method for identifying individual chemical moieties interacting with a target molecule via PCR. Support for these claims can be found in the originally presented claims 22, 24, and 25 respectively. Further support for these embodiment can be found, for example, in lines 32 to 35 on page 19, in lines 13 to 18 on page 19, and in the paragraph bridging pages 19 and 20 of the specification respectively.

Claim 37 is newly presented to set forth a preferred embodiment of the method for identifying individual chemical moieties interacting with a target molecule via hybridization. Support for this claim can be found in the originally presented claim 27. Further support for this embodiment can be found, for example, in the paragraph bridging pages 18 and 19 of the specification.

Claims 38 and 39 are newly presented to set forth preferred embodiments for the method of deconvoluting the specific combinations of chemical moieties that bind a target molecule with the greatest affinity. Support for these claims can be found in the originally presented claims 28 and 29 respectively. Further support for these embodiments can be found, for example, in lines 10 to 18 on page 19 of the specification.

The Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

Response to the Restriction Requirement

The Applicants elect Group I with traverse: Claims 1 to 7. Applicants note that the claims are drawn to combination reaction products of the recited chemical compounds. Applicants specifically request rejoinder of Group II which is drawn to libraries having members of the compounds of claim 1. The Applicants also request rejoinder of Group III which concerns the use of the products of claim 1. Accordingly, as all the claims set forth the same inventive technical feature of a combination reaction product, their rejoinder should place no undue burden on the Examiner and is in full compliance with the governing regulations.

No election of a species was required in the Action. If one is required, the Applicants would elect the species of oligonucleotide self assembly moieties.

We next respectfully traverse the basis for imposing the restriction requirement and present, for your consideration, a summary and analysis of the cited art in support of our position that the cited art does not negate the Unity of Invention.

A. The Winkler Art

The Winkler et al. art, US 2004/0058373 A1, discloses a method of comparing the relative abundance of specific mRNA molecules from a plurality of different sources. In order to do so, all mRNA molecules isolated from a single source are amplified via various methods and then tagged with exactly one species of a nucleic acid molecule comprising amplification and differentiation domains, herein referred to as the "source identifying nucleic acid tag". The tagged molecules from all of the sources being compared are then mixed together and fractionated via the inherent nucleotide sequence encoded by the mRNA molecule, as opposed to the sequence provided by the source identifying nucleic acid tag sequence. Individual mRNA sequences of interest are then selected, and expression levels of said mRNA sequences are relatively compared between sources by amplification via their source identifying nucleic acid tag.

The Winkler et al. art varies quite distinctly from the subject matter of the instant claims with respect to compositions and their use. Insofar as the Winkler et al. compositions themselves are quite different from those now set forth in the claims, the Applicants will focus only on the differences between the compositions.

The composition of the tags in the Winkler art and of the instant claims vary in a critical fashion. In the Winkler art, the tag comprises *amplification* and *differential* domains, whereas in the instant claims, the oligonucleotide further comprises a *self assembly moiety* which serves to join the chemical compounds of the combination reaction product of the claims together. These products bring two separate chemical moieties in close proximity to each other in order to mimic a single compound containing both of said chemical moieties. The self assembly domain of the claims *would actually serve to inhibit* the intended function of the tag in the Winkler art. If oligonucleotide self assembly moieties were included in the oligonucleotide tags taught by the Winkler art, separation of individual mRNA species, via their inherent encoded sequence, would be hindered by the oligomerization of different mRNA species by means of said self-assembly moieties. It is to be also noted that the subject matter of the instant claims are further distinguished from the Winkler et al. art insofar as the claims are drawn, at least in part, to *combination reaction products* wherein the at least two chemical compounds are bound to each other by their respective self-assembly moieties. Such products are simply not found in the Winkler art.

Secondly, the Winkler art teaches of a source identifying nucleic acid tag in which, "The differentiation domain for each sample are unique to that sample.", as stated in paragraph [0013]. Said sample to which the tag is affixed to is further defined in the art as follows; "Nucleic acid samples are collections of RNA and/or DNA…", in paragraph [0077]. Since "collections of RNA and/or DNA" imply more than a single species of nucleic acid, the source identifying nucleic acid tag is affixed to a plurality of nucleic acids containing divergent sequences, and therefore is not unique to a single chemical moiety. Specifically, Winkler et al. states in paragraph [0021] that, "the advantages of the invention allow one to analyze a variety of nucleic acid targets in the samples… Therefore, in many instances, the first nucleic acid target will be only one of a plurality of nucleic acid targets…" Plurality is later defined in paragraph

[0059] as "more than one. In certain specific aspects, a plurality may mean 2, 3,... 150,000, 200,000 or more..." This is in stark contrast to the instant claims which set forth a unique nucleic acid tag for every unique chemical moiety of the product.

The use of the tags in the Winker art and instant claims are also quite distinct. In the Winkler art, as described above, the tag is ultimately used to compare the relative amounts of specific mRNA species from differing sources, which are distinguished by the source identifying nucleic acid tag. Whereas in the instant claims, a first, self-assembly moiety 'tag' is used to first create a plurality of combinations of different chemical moieties, which as described above would be disadvantageous for the applications taught in the Winkler art, and a second, oligonucleotide 'tag' is used to identify the unique chemical moieties bound to said first 'tag', as opposed to only identifying the source of the chemical moiety as taught in the Winkler art.

Finally, the utility of the applications taught in the Winkler art and instant claims are highly divergent. The ultimate utility of the Winkler art is the ability to compare the relative abundance of a particular nucleic acid species across a plurality of sources and to determine nucleic acid profiles of limited tissue samples. The Applicants, for instance, claim methods directed toward identifying combinations of different chemical moieties that bind to a given target.

Accordingly, as the Winkler art does not teach or suggest all the elements of the Applicants claims, the Winkler et al. art can not negate the novelty of the Applicants' claims.

B. The Burmer et al. Art

The Burmer et al. art, US patent No 6,087,103, discloses methods of screening ligand binding to one or more target molecules. In this art, a library of oligonucleotide tags is bound to a library of ligands such that each individual ligand is affixed to an oligonucleotide tag comprising a unique sequence. The resulting plurality of tagged ligands can then be simultaneously screened for binding to one or more targets, and identified via the unique sequence comprising the oligonucleotide tag.

The Burmer et al. art varies critically from the instant claims in the composition of the oligonucleotide tag. Burmer et al. disclose a tag which "refers to a molecule with a

recognizable feature that allows it to be distinguished from other tag molecules.", as found in the second sentence of the Definitions section. Burmer et al. neither disclose nor suggest an self-assembly domain as set forth in the Applicants' claims which serves to bring two separate chemical entities in close proximity to each other in order to mimic a single compound containing both of said chemical moieties. This provides a distinct improvement over the invention described in the Burmer art. Namely, that given the same library of ligands as described in the Burmer application, the screening capacity related to the instant claims would be exponentially larger.

As an example of this distinct advantage, take a library of ligands as taught in the Burmer art, containing 384 unique chemical moieties. If said ligand library was tagged as described in the Burmer art, then a single screening reaction with a given target molecule would encompass 384 potential combinations of target and ligand. Now if that same ligand library was tagged as described in the instant claims, a single screening reaction with a single target would encompass 147,456 (384 x 384) potential combinations of target and ligand. This is due to the unique feature of the instant claims, namely the self-assembly moiety contained in the oligonucleotide tag, which allows for a plurality of combinations to be generated by bringing two separate chemical entities in close proximity to each other in order to mimic a single compound containing both of said chemical moieties.

Accordingly, as the Burmer et al. art does not teach or suggest all the elements of the claims, the Burmer art can not negate their novelty.

Insofar as both the Winkler et al. and Burmer et al. references lack the self-assembly moieties of the instant claims, and especially as these references each fail to disclose combination reaction products as set forth in the claims, a combination based upon the disclosures of these two references can not provide all the elements of the claims and thus can not negate the nonobviousness of the claimed subject matter.

Accordingly, the Applicants respectfully request reconsideration and withdrawal of the Restriction Requirement and rejoinder of all three groups.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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